produce a musical murmur it was believed necessary for the surfaces over which the blood stream passed to be quite smooth. Dr. Meyer estimates the frequency of murmurs audible at a distance from the chest as perhaps 1 in 300 cases of heart disease.

NOTE.—At a meeting of the Section following that before which the case here reported was presented Dr. H. A. Hare exhibited a case of aortic insufficiency with a diastolic musical distance murmur.

THE FLUORESCENCE OF QUININE AND OTHER REMEDIES IN THE CURE OF MALARIAL FEVER.

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IN a recent paper[*] it was maintained that the malarial parasite would not sporulate in the dark; that the light it obtained in the blood was necessarily *red;* and, following the demonstrations of Harrington and Leaming,[1] that *amœba proteus* streams in the presence of *red* light and ceases to stream in *violet* light, it was assumed that the same may be true of the *malarial* amœba; hence it was suggested that the curative action of quinine might be due to its fluorescence, producing violet rays of light in the blood. Evidence in support of this view will now be presented

First, it may be noted that two other vegetable products possessing blue fluorescence in a remarkable degree have long been known as effective remedies for intermittent fever, viz., esculine and fraxine (or fraxinine).

As to the efficacy of esculine former records furnish abundant testimony. Notably, Monveneux[2] reports in detail twenty-eight cases successfully treated, a report the reliability of which is accentuated by the author adding ten other cases which esculine failed to cure, but which were promptly relieved by quinine.

An article in the *French Dictionary of Medical Science*[3] refers to the experiments of MM. Mouchon, Durand de Lunel, Diday, Vernay, and Monveneux, as demonstrating that esculine is comparable to quinine as an antiperiodic. The bibliography at the end of this article contains twenty-three references to esculine, dating from 1720 to 1858.

I find esculine presents, in solution, a far more brilliant blue fluorescence than any salt of quinia or cinchona. Its fluorescence is, however, immediately destroyed by dilute sulphuric acid, but promptly reappears by adding a few drops of aqua ammoniæ to the solution.*

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[*] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, February, 1902.

Fraxine—the other fluorescent substance named—is made from the bark of *Fraxinus excelsior*, the common ash tree of Europe. This was often given successfully for intermittent fever before the discovery of quinine, and later, one writer who reports cases cured by it, in which quinine had previously failed (?), was so convinced of its efficacy that he surnamed it *quinquina d'Europe.*[4]

The tincture and other preparations of *iodine* have been used successfully for intermittent fever for a long time. The literature on this subject is extensive. Sircar[5] gives seven successful cases, and quotes Grinnell[6] to the effect that " one hundred and forty cases were treated with the iodine, and the results were fully equal to those treated with the sulphate of quinine. The remedy seemed to act almost as by magic," etc.

Now, while iodine is *not* fluorescent, and cannot, therefore, act (as suggested for quinine) by accentuating violet rays, yet in the body it can scarcely escape coming in contact with starch and forming the *blue or violet iodide of starch*, which is all the more likely to occur from the iodine being usually given *after meals*, to avoid its irritating effect on an empty stomach. Thus the curative influence of tincture of iodine would seem to fall in line with that of Prussian and methylene blues. One writer, Entrikon,[7] prescribed the *iodide of starch* itself, but finally settled upon the compound tincture of iodine as the best of several preparations.

While the antiperiodic effect of the fluorescent substances esculine and fraxine favor the idea that fluorescence may be the curative property in quinine, the proof is insufficient. We need direct experiments showing that quinine actually produces fluorescence in the body, and that coincidently the symptoms and phenomena of malarial fever disappear.

Exactly these results were actually obtained more than thirty years ago (1868) by the experiments of Drs. Edward Rhoads and William Pepper, of Philadelphia. These experiments, so long buried in oblivion apparently, were brought about in the following manner: In 1866, Henry Bence Jones,[8] experimenting on the rapidity with which medicinal substances pass into and out of the body, was induced to use quinine for this purpose on account of the extremely minute quantity of this substance (1 grain in 1,000,800 parts—nearly 117 litres of water) that could be recognized by its fluorescence. To his surprise, he found that fluorescence existed in the blood and most of the tissues of man and animals in those who had *not* taken quinine, but it was increased in those who *had* taken it. Without following him in detail, Jones obtained the result—interesting to us now—of discovering a substance in the tissues of guinea-pigs and man which possessed *all* (*italics* his) the chemical and optical properties of quinine, including fluorescence. He called it *animal quinoidine.* Early in his paper Jones remarks: "No imagination could have anticipated that this line of research into the rate and passage of substances into and out of the textures would lead to the supposition that man and all animals possess, in every part of the body, the most characteristic peculiarity of the bark of the cinchona trees of Peru;" and later in his paper he says: "Assume that a substance like quinine exists during health in the textures, can its rapid destruction and removal through the action of the marsh miasm* give rise to ague?"

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* I obtained the drug from Merck & Co., of New York, who, in their "Index" for 1896, p. 93, describe it as an "antiperiodic. Uses: *Instead of quinine for intermittent fever.*" They inform me that little is sold, probably from its high price—three cents per grain.

Following Jones, Drs. Rhoads and Pepper[9] endeavored to determine "whether there might not be, as an attendant upon the pathological processes in malarial disease, a rapid and marked diminution in the amount of 'animal quinoidine' naturally existing in the tissues."

They first repeated the experiments of Jones and corroborated his results, and then proceeded to test the blood of malarial patients, with the result of finding its *fluorescence below the normal standard.* Altogether they give twelve cases, amply described and tabulated. They obtained blood by cupping over the spleen, and the degree of fluorescence was determined by comparison with the fluorescence of standard solutions of quinine of known strength—a given number of grains in 100 litres of distilled water. Thus a fluorescence of 3 would equal that of a quinine solution having 3 grains of quinine in 100 litres of water; a fluorescence of 6 would equal that of 6 grains in 100 litres, etc.

Their twelve cases may be epitomized with extreme brevity, as follows: Case I. Healthy woman. Fractured bones. Blood-test gave fluorescence of 3. Case II. Tertian ague; fluorescence, 1½. Case III. Marked intermittent; fluorescence, 1. Case IV. Marked intermittent; fluorescence, ⅛. Case V. Tertian; fluorescence, ⅛. Case VI. Quotidian; fluorescence, ¾. Case VII. Quotidian and tertian; fluorescence, ¾. Case VII. Quotidian and tertian; fluorescence, ⅗. Case VIII. Tertian; fluorescence, ⅜.

These cases show a fluorescence of 3 in the normal woman, and of less than 1 in five of the seven cases of fever, the other 2 being severally 1 and 1½. In these seven cases no quinine was given, and care was taken to ascertain that none *had* been given for some days before the examination.

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* This was thirty-four years before Laveran discovered the malarial parasite in 1880, and before the part played by the mosquito in malarial disease was recognized in 1883.

Then follow 2 cases showing increase of fluorescence and consequent cure by sulphate of cinchona.*

Case IX. Quotidian; fifteen months' duration; spleen enlarged. Fluorescence: "*none* could he discovered, and it was doubtful if any existed." After fourteen days under cinchona sulphate no recurrence. Much improved; fluorescence, 1¼.

Case X. Quotidian for nine days following previous irregular symptoms. Fluorescence, ¾. After six days, cinchona sulphate 20 grains daily; fluorescence, 3½; no recurrence of chill.

Next come two fatal cases. One (XI.) was a quotidian of four weeks' duration. Last two paroxysms congestive; the final one at 11 A.M., death at 2 P.M. Had taken 20 grains of cinchona sulphate two days before death, and one or more doses of 15 grains each on the day of decease. Post-mortem examination revealed fluorescence of 2½ in blood of spleen and 2½ in blood of liver.

Case XII. Chronic malarial cachexia; ten months' duration; general dropsy three months; improved under cinchona and Basham's mixture, then typhoid fever, and death on ninth day of that disease. Took *large doses* of cinchona for *fifty-four days* preceding demise. Fluorescence in blood of spleen, 6, and of liver, 8.

At the conclusion of their paper the authors remark that their observations "indicate, by the uniformity of the results, a close connection between the diminution of 'animal quinoidine' and malarial disease."

In 1875 Mills,[10] of Philadelphia, suggested that fluorescence may afford an explanation of cinchonism. Commenting on the experiments of Jones, Rhoads, and Pepper, he says it has been proved that animal fluorescence is increased by quinine; that it "is decreased below a normal standard in malarial affections, and that it rises in the scale *pari passu* with the giving of the cinchona preparations and the improvement in the symptoms of the diseases."

Thus, then, it is the peculiar relations of the cinchona preparations *with light* that give a clue to the explanation of their curative effect. Possibly the same may be said of *all* assimilable substances that fluoresce a *violet* or *blue* color. Some substances have a green, orange, or red fluorescence; these we should not expect to have any curative influence in malarial disease.

It remains to explain the cases in which quinine *fails* to cure—exceptions that seem to prove the rule that the malarial organism will not sporulate in the dark, and, further, that *in* the dark quinine (necessarily) cannot kill the parasite with fluorescent *light*.

In these cases the febrile paroxysm is not produced by the usual tertian or quartan parasite, but by the "malignant" crescentic form of which Manson[11] gives three varieties, viz.: 1, æstivo-autumnal; 2, malignant quotidian; 3, malignant tertian. He calls all of these crescentic forms "malignant infection," and says "the malignant parasites *alone* form crescent bodies" (p. 65): that quinine "has apparently no influence on these bodies" (p. 66); they "may be found for days after the patient is cinchonized" (p. 44); or, "after full doses of the drug continued for a fortnight" (p. 183). The malignant parasite does *not* cause fever paroxysms, but is usually associated with marked cachexia" (p. 66); all of which is explicable by the further facts that "these crescent parasites are not generally found in the *peripheral* circulation" (pp. 15, 65, and 85), where they can get *light*, but *are* found in the spleen, liver, bone-marrow, and brain, than which no *darker* recesses of the body can be imagined, and consequently where the fluorescent property of quinine *must* be impotent. When they *do* appear in the peripheral circulation "it is a sure sign that a paroxysm of fever is impending" (p. 69); that is to say, having come out of their dark recesses into the red light of the peripheral blood, sporulation occurs, and with it the usual ague paroxysms. These quinine may arrest, but it cannot act upon parasites in the dark.

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* *Cinchona* sulphate was used instead of quinine. Authors do not state why. Probably the quinine salt may have been too expensive for hospital use in those days.

Possibly the malignant parasites are sickly, degenerate, or famine-stricken individuals, from the man's blood being overstocked or anæmic. The corpuscles containing them are *not enlarged* like those containing benign tertian parasites; the latter may be sometimes nearly twice the diameter (Manson, p. 62) of healthy corpuscles.

A normal capillary will just admit one nornal corpuscle to pass, and while both are elastic, and the skin capillaries among the largest in the body, it is conceivable that the enlarged corpuscles with benign tertian parasites *become arrested* in the skin, on account of their size, and so remain until light causes them to break up by sporulation; on the other hand, the smaller corpuscles with crescent parasites are *not* arrested in the skin capillaries so as to be continuously exposed to light, but pass on and become arrested by smaller capillaries in the brain or elsewhere. Some of them may eventually get light enough to manage sporulation, at odd times, or continuously, but not a sufficient number sporulate *simultaneously* to generate a fever paroxysm.

In a normal case of typical tertian ague the successive events that occur during the three stages of chill, fever, and sweat are as follows: Previous to the chill a group of corpuscles lies arrested in the peripheral capillaries, their parasites exposed to sunlight preparatory to sporulation. With the sporulation is the *chill*, by which the skin arterioles are violently contracted and emptied of blood; hence, pallor and coldness of the surface; and, as if to assist in the dislodgement of the infected corpuscles and their complete disintegration, the whole fabric of the man's body vibrates with a "shaking chill." During the *fever* the arterioles dilate again, even beyond the normal limit; an actual congestion of the skin occurs; hence its redness and heat, during which a new crop of infected corpuscles enters the peripheral capillaries. During the *sweat* a deluge of water exudes from the distended cutaneous bloodvessels, causing them to contract, close up, and shut down upon the new group of infected corpuscles, which, thus arrested, so remain until forty-eight hours of sunlight secures in turn their sporulation and the recurrence of another paroxysm. Thus a typical tertian paroxysm might be regarded as a *functional disease* (or process) *of the skin*, during which the human organism is operating, according to nature's laws, in the interest of the parasite to secure perpetuation of its species. If the process were allowed to run its natural course without interruption (without clothing, quinine, etc.) the human individuals, or their race, in the course of many generations, get their compensation by becoming black from malarial melanosis, with the same immunity that now belongs to dark-skinned peoples.

Thus regarding the malarial process as *naturalists* instead of *medical practitioners*, this new point of view presents confirmatory evidence of the rôle played by sunlight in producing the observed phenomena.

Finally, the idea that succession paroxysms of fever are produced by sporulation of successive groups of those parasites *only* whose domiciliary blood-corpuscles have become sufficiently enlarged to cause their arrest in the cutaneous capillaries is, I am aware, at variance with the generally recognized theory of Golgi that the paroxysms are produced by successive *generations* of parasites, each fit corresponding to the ripening, sporulation, and setting free of a *new brood*.[12] My idea is that only such a *part* of any generation, the blood-corpuscles of which have become large enough to get arrested in the peripheral circulation, sporulate at any one paroxysm. The others must take their turn, waiting until the corpuscles they inhabit have become increased in size sufficiently to get arrested in the skin, where sunlight may be obtained to secure their sporulation also.

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A STUDY OF HYPERPLASIA OF THE PHARYNGEAL LYMPHOID TISSUE (ADENOIDS), WITH ESPECIAL REFERENCE TO PRIMARY TUBERCULOSIS OF THE PHARYNGEAL TONSIL.

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Introduction. The most important recent literature on the pharyngeal tonsil relates to tuberculosis of this tissue. While many of the newer investigations have thrown considerable light on the morphological and clinical aspects of the lesion, numerous points still remain to be settled. Perhaps one of the most interesting of these at present is the frequency with which this lesion occurs, and whether or not the lesion remains focal or may become disseminate. Thus far the results of study as to the frequency of the lesion permit of widely different interpretations; and in order to throw further light on this point we have restudied the question in a systematic manner, and have, in the course of our investigations, incidentally touched upon certain questions related to the bacterial infection and general pathology of adenoids.

The Normal Tonsil. Considered either from the anatomical or physiological view-points, the various lymphoid tissues of Waldeyer's ring present fundamental features in common. Their morphology and function have best been studied in the faucial tonsil; and only very recently, and to a much less extent, have similar observations been made on the pharyngeal lymphoid tissue.

The tonsils are composed of lymphoid structures closely resembling in their general anatomy Peyer's patches of the small intestine.[1]

The physiological activities of the tonsils have been variously interpreted by different investigators. The older view, now discredited, assumed that they were secreting organs furnishing a thick, viscid mucus. Later, Kingston Fox,[2] Hill,[3] and Spicer[4] advanced the view that these structures reabsorb the waste secretions of the neighboring

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[1] For a consideration of the anatomy of the normal pharyngeal tonsil, with bibliography, consult Gottstein and Heymann's Handbuch der Laryngologie und Rhinologie, Wien., 1899, Bd. ii. S. 534.

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[4] Spicer. Lancet, 1888, vol. ii. p. 805.